intent of the product is to say that heroin use, understanding that it's specifically for heroin, heroin use can be detected within the last 90 days, then I think you do have to answer this question, because you need to know whether or not you really would have been able to detect heroin use if it's a single use within the last 90 days. I mean I'm fairly open on this issue. To me it depends on what do you want to do with that result and what are you going to say about that result?

So, again, to me, it's an interpretation issue or an ability to provide adequate interpretation issue for a positive or a negative result, whichever way it goes. Was there -- you know, if they use a lot, will you be able to detect it? If they use only once, will you be able to detect it? I'm not even suggesting that you, and I'm certainly not suggesting that we, go out and administer heroin to non-drug using volunteers and give them heroin or even drug-using volunteers and give them heroin.

I think that they're perhaps getting back to our -- this directly relates for me to the other

question that you can design a perspective study that is well enough statistically controlled, I think, in the data analysis to do this without having to administer necessarily controlled doses to non-using drug volunteers to answer this question.

So, if the intent is to be able to make statements about your ability to detect individuals as positive or negative, and I think you need to know the minimum dose required to product a positive result.

DR. KURT: Tom Kurt. I agree in part with that, but I think this is best left up to an advisory board that reviews on this particular topic, such as the DOT cutoffs were set by an advisory board specifically set for such and Dr. Selavka who was here earlier with his Hair Testing Working Group could very easily set up a kind of a working group in that kind of a situation to review this exact topic based upon the existing scientific studies, taking into account what would be considered a rather substantial use, which I think in part has been explained in the sponsor's application.

DR. KROLL: Martin Kroll. I have a

tendency to like to see that the minimum dose and detection of any system is determined sort of independent of the matrix. Now, I understand there's a lot of ethical issues; you don't want to give heroin to people. But you do appear to have information that can relate the amount of morphine. That way you could detect versus the amount of the MAM in hair.

And there are certainly plenty of people who take morphine for medicinal purposes where it could actually be fairly well controlled. You know what the exact dosage would be. So, it might be appropriate to use something like that as a surrogate to get at least an idea so that if somebody was interested in what the minimum dose was, that there would be some reliable information.

DR. MANNO: Barbara Manno. I think I heard something earlier today concerning the fact that this test is really a test to detect chronic use of heroin versus it's not so great for acute use. And looking at the pharmacokinetics, assuming that this is -- this is a big assumption, I know -- but that the first test, the RIA test, as proposed here, would be

confirmed knowing that you have such a short window of detection of 6-MAM in urine, I'm wondering if we don't need to know when that's going to show up in hair, which then reflexes back. >From that standpoint, we're going to need to know when an approximate minimum dose to give us a positive.

There's a second issue that I don't see -- I did not remember seeing, but here again is addressing just the assay itself, and that is what's the LOD and the LOQ of the procedure itself, both within day and between day? So, there's really two issues to determine whether -- you don't know what you're looking for to start with without those two things. And -- yes, that's all I have to say.

DR. LEWIS: Sherwood Lewis. I don't think that it's at all reasonable to even talk about minimal doses when we're dealing with heroin. This is not like conducting a controlled clinical trial where you give the particular drug or medication under known conditions, quantitatively, and then look for whatever the results might be, if their analytical results, by drawing blood samples, what have you.

So, to me, it doesn't have any meaning. Knowing the notorious nature of the material itself and the roots of administration with regard to heroin, I don't know how you could even begin to talk about minimal doses or any other doses in that respect.

DR. CLEMENT: I concur with Dr. Lewis. I think the sponsor showed a negative threshold between their sensitivity of doing the test, the two nanograms, to pick up chronic heroin users, but still is high enough so it does not pick up poppy seed users.

I guess my ignorance of not being familiar with the toxicology is whether or not cough syrup and codeine and cough syrup and other forms of codeine can counteract particularly on a MAM test, but I'll be interested in the sponsor's comments or any of the other panel's comments on medicinal amounts of codeine can be found positive both on the urine test and the confirmatory.

DR. KROLL: We can try to clarify that now.

MR. IRVING: Hi, I'm John Irving. Codeine

does not produce 6-MAM in either hair or urine. It's a specific metabolic product from the use of heroin. There's no way the body can produce 6-MAM other than that.

DR. CLEMENT: Okay. Thank you. Well, in that case, I think the sponsor's done a sufficient job on clarifying the sensitivity based on the studies available and it's within a sufficient range.

DR. HENDERSON: Cassandra Henderson. From the materials submitted, it was clear that MAM was only produced if a person ingested or used heroin in some manner. So, as a clinician, I don't really care what the minimum dosage is. If it's there, it's there, and that's all I need to know.

DR. ROSENBLOOM: Yes, I agree. This is an illegal drug. If it's there, it's there. I don't think -- a minimum dose required to get a positive result might be interesting and someone might want to do a study in legally administered morphine, but I don't think -- oh, it's just in heroin, yes, so there is no legal heroin. So, I don't know how it could be done or why it would need to be done.

DR. LASKY: I agree. It's the obligation of the sponsor to demonstrate that their cutoff point is analytical supportable, and that's the limit of what this test is designed to do, and which that also addresses question number 4, in my opinion. Trying to move ahead.

(Laughter.)

MR. REYNOLDS: And I agree with Dr. Rosenbloom and Dr. Henderson that this is an illegal drug. There's no level that's acceptable. It doesn't really matter whether you're talking about a low dosage over a period of days or weeks or a large dosage over the course of a weekend. If it gives you a positive, it gives you a positive, and it doesn't matter how the positive got there. Whether it was chronic low dosage or short-term high dosage, a positive is a positive. So, I don't think it's really that critical. I think that they've established their detection limit, and that's the only thing that's really pertinent in this area.

DR. EVERETT: James Everett. Certainly, I think the minimum dose should be detected or

determined, which they have. And that's very important for any test that you do. You must know what the detection limits of that test really is. Because this is test performance we're talking about, and this is the real reason for detecting things that might cross-react with your test.

It's when your lab results fall outside of that range, you have to question whether the test is accurate or not. And without those detection limits, you have no real recourse for knowing whether you're dealing truly with an instrument failure, procedure failure, a technician failure or in this particular case something the patient or the client may have done to their hair.

And in a real-world situation -- I am family practice, and I see tests all the time that are incorrect. They don't necessarily agree with what the patient says. but in essence the question becomes who do I believe the test or the patient? And the first thing I look at is the parameters of the test. What did the manufacturer say the test is capable of doing, and then I move on to evaluate whether or not the test

truly is positive or whether it's a false positive.

But, in essence, without looking at the patients, if you're going to have a test, that test must have performance parameters, and you must know what that test is capable of doing, if for no other reason than to determine if the test is capable of doing what the manufacturer says it can do.

DR. KROLL: All right, thank you. Let's go to question 4.

DR. PEACOCK: Question 4: Should the relationship of the pharmacokinetics of drug use and the incorporation of drug into the hair, that is single dose, multiple doses, and chronic use, be determined?

DR. KROLL: Okay. Let's start with Dr. Lewis, and we'll go --

DR. LEWIS: Yes, I'm still mulling over my response to question 3. I read that as meaning minimum dose, literally dose, not detection limits, as Dr. Everett was speaking. I certainly agree with him on that.

And I would say that for question 4, to

get on with it, it would be nice, but I don't think that it's necessary this purpose to have that pharmacokinetics information.

DR. KROLL: Okay, and let's move clockwise. Dr. Manno.

DR. HENDERSON: Should we move back just briefly to 3 to comment on Dr. Everett's interpretation of 3 that it's the parameter of the test? And I think Dr. Lewis and certainly I thought that it was how much drug does a patient have to take in order to get a positive result. And I don't care. I mean whatever they take is -- but Dr. Everett's point is that the parameters of the test need to be identified and specific that you can go to the packet insert and everybody knows what the test measures and what the cutoffs are.

DR. KROLL: Okay. Maybe Dr. Peacock can clarify this question and whether we've answered it adequately.

DR. PEACOCK: We were thinking about the dose required, especially with the 6-MAM and the morphine. You know, you might -- it goes back to the

variation, you know, we were worried about for hair, bias to hair color as well, that it was related to the dose of drug being taken, not the performance of LOD.

DR. ROSENBLOOM: I think that's the way most of us read it.

DR. KROLL: Dr. Manno?

DR. MANNO: Barbara Manno. Like the physicians, I don't care if a person took a single dose, multiple dose or they're chronic users, but what I do concern myself with from the laboratory standpoint is did the sample get collected in the right time frame relative to drug use, and that gives me -- I'm more concerned about that aspect of the pharmacokinetics at this point than I am anything else. So, a full pharmacokinetic profile I don't think is necessary in order to say whether the test is working or not.

DR. KROLL: I tend to agree with Dr. Manno. I think if there's information in literature or other studies, if they can be put together in a very nice review and they can be modeled some sense to show how different types of patterns or drug use over

different periods of time how that would get incorporated in here and what you expect to see, that that would be adequate.

DR. KURT: Tom Kurt. Because this is a testing for chronic drug use, I think the pharmacokinetics is somewhat of a moot point, except as Dr. Manno pointed out, the sample needs to be collected proximate in time. It's nice to know that there are other metabolites that are captured by the hair, such as the 6-MAM and are there, but I think it's important to rate this as a chronic test, and perhaps in the future it could be used in companion with the an acute test, such as a saliva test.

DR. WILKINS: I agree with the previous speakers, Dr. Kroll and Dr. Manno and Dr. Kurt, what they just said. And I'd like to say that I don't think full-scale pharmacokinetic studies are necessary for chronic use. However, again, to me, to my mind, just as a panel member, it's going to totally depend on what the claims are that are going to be made. And in my mind, if the claims for the consumer or the clinician is going to rely on this test to assist them

in making a determination of drug use or whether, a treatment intervention is necessary or whatever.

And as it's been pointed out by the panel member, what they really want to know is, is this -- if I've got a positive, I'm fine. Well, great. So, are you always going to find if somebody takes heroin, how is the test going to be reliable enough to determine that this person took heroin and I can detect it? And am I going to pick up every positive, and am I going to accurately determine the negatives?

And I think to some degree you can't really -- I don't think that the data that I've seen has really answered that question for me, that if you get a negative result, for example, that that means the person has not used heroin, okay, totally. And I realize that's an issue of false negatives and false positives, but for most products you're looking at sensitivity and specificity, and I need more information for that, I think.

The other issue that hasn't come up yet, but really to me relates directly to questions 3 and 4 in a way, is that the one thing that I haven't seen

yet, and again the sponsors may have the information, is for 6-MAM, if this test is intended to be used for heroin use.

Just a simple question: If you have a hair sample or hair from a donor and you analyze that hair sample 20 times from the same donor, do you always get the same -- how does that relate to your cutoff and the positive result, not standards or controls but a donor whose hair contains drug, and you analyze that over and over again? Can I rely on the fact that if I get a positive result this time, I'm going to get a positive result the next time and the next time?

That's the reproducibility of the test system that I don't think we've talked about at all, and I may have missed that. But to me that relates to questions 3 and 4 and the ability to interpret a positive result of the test.

MR. IRVING: My name is John Irving again. Let me put this in perspective. If I'm a drug user, a heroin user, and I get collected now and I'm positive, I get collected four hours from now, I'm

negative.

DR. WILKINS: That wasn't the question.

MR. IRVING: I know. If I take a hair sample now and I repeat the sample numerous times, I'm going to get a positive. If I collect the sample tomorrow and an individual was right off the cutoff, I'm going to continue to get a positive. So, we are going to get a much more -- I'm not sure exactly what your question is.

DR. WILKINS: I don't think that that answers -- I'm just saying if I take a heroin user's hair sample and take a sufficient sample that I can analyze that same pool of their hair or specimen that is received by the laboratory multiple times --

MR. IRVING: I think that that is in the submission.

DR. WILKINS: -- on the same sample -- well, I haven't seen any data. That's why I'm asking the question, on hair, not --

MR. IRVING: It's in the submission we passed on to the FDA.

DR. WILKINS: Okay. Because that was one

of the questions I had is for 6-MAM how reproducible is that? And if you have a sample that's around your cutoff -- it's defining the issue of positive.

MR. IRVING: We had data in there that provided that information, and --

DR. KROLL: Excuse me, Dr. Gutman wants to make a comment.

DR. GUTMAN: Yes, that's not a review issue. We have that information and didn't think it was a problem.

DR. WILKINS: It may not, but for me to answer these questions I felt that that was something I needed to know.

DR. GUTMAN: Diana, it's in the submission under physician data. We went even as far as taking the sample, testing it a year later, the same sample, and got comparable results. That's in the submission. We took the sample and --

DR. WILKINS: No, I thought some of those decreased over time, didn't they? But that's a different issue.

DR. GUTMAN: A slight decrease.

DR. WILKINS: Okay.

DR. GUTMAN: It's within experimental range, but that was also part of that submission.

DR. WILKINS: Okay.

DR. GUTMAN: So, yes, we will continue to get a positive on that sample.

DR. EVERETT: James Everett. I don't think the pharmacokinetics under these conditions is truly necessary. But I didn't read anything in the papers that we got that described whether the hair was incorporated -- whether the drug, rather, was incorporated into the hair uniformly in its distribution. And that is did they have a particular site where they thought the hair sample should be taken from; that is, is it incorporated in the back of the head the same rate as it is in the front or the side? I didn't really see that.

DR. HENDERSON: It's there.

DR. EVERETT: It's there?

DR. HENDERSON: It's there.

DR. EVERETT: Okay.

DR. KROLL: Stan Reynolds?

MR. REYNOLDS: Stan Reynolds. And I pretty much agree with the rest of the panel that basically I don't think you need to do pharmacokinetics. Again, there's the problem with how would you do it if you wanted to unless you could compare it to morphine or something else.

Basically, what I need to know and what people using this need to know is if an addict took heroin yesterday, can I pick it up today? It's that simple. Or can I pick it up tomorrow. What's the time frame from the time of use that you can pick it up? I think that's what we all need to know. It goes back to the sample collection. When I can be sure that the sample from a user actually is going to become a positive? Is six hours too soon? Is eight hours enough? I think that's the basic information that you want.

DR. HENDERSON: That's in the submission about it depends on the rate of hair growth. It's in the submission, and it depends on the rate of hair growth, that I think it was 0.6 millimeters to, I think, four millimeters was the length that I read,

and from 14 days to 90 days. So, that's in there. And the reproducibility I think is in there where they stored it for a year and then tested it again, and that was similar.

DR. LASKY: Fred Lasky. This is not necessary for the submission, in my opinion.

DR. ROSENBLOOM: Arlan Rosenbloom. I would like to know -- I think it would be interesting to know if a single-dose exposure -- say a kid goes to a rave and two months later if it's in his hair or her hair. I think that would be interesting. I'm not sure how important it is for workplace testing and all the other applications.

It would seem to me that -- and this is not a pharmacokinetic issue as much as how much exposure you need to get a positive test -- I would think that the differences in usage would be worked out by the MRO who's reviewing this data with the user and if they say, "Well, I'm not using it anymore" or "That happened six months ago," is there a possibility of looking at the hair segmentally to get them by the short hairs, as it were, and determine whether they've

had drug use in the last month or so? Perhaps the Company can comment on that.

DR. CAIRNS: I regretted, perhaps, to educate you to the science of hair testing. Yes, hair grows half an inch per month. And as regards the ingestion to the hair appearing at the surface of the scalp for cutting, that would take between five and seven days to grow from base of follicle to surface of skin for cutting. So, your question is that if someone took heroin today, yes, it would take seven or perhaps a few days longer for that section of the hair that the heroin is incorporated in to be cut from the scalp and tested.

For the issue of segmental analysis, that is correct, you can in fact look at, say, that first half-inch of growth from the scalp which will detect the drug use within that 30-day approximate time window. The minimum detectable dose, we've outlined in the submission as a mean detectable dose of 173 milligrams per month. And that's an infinitesimally small amount compared with, say, a chronic user up at 800 milligrams per month.

DR. ROSENBLOOM: These doses mean nothing to me. That's not a --

DR. CAIRNS: But you're correct, it can be detected in a shorter length of hair.

DR. ROSENBLOOM: Does a dose like that, as a single dose, I mean does that make sense as a single dose, number one? Number two, if it does make sense as a single dose, then it would appear, I presume, in a segment.

DR. CAIRNS: Well, a single dose, Dr. Rosenbloom, may well be only somewhere of the order of 16 or 20 milligrams, if you're talking street dose. In that case, the individual may have to consume several little doses to go just above the cutoff.

DR. ROSENBLOOM: So, the problem of picking up a single dose is you likely wouldn't.

DR. CAIRNS: Yes. We stress the fact that the reason for not doing the single-dose study was an analytical problem, that a single dose would not challenge the assay or the cutoff.

DR. ROSENBLOOM: Okay.

DR. HENDERSON: I have nothing to add.

Cassandra Henderson.

DR. CLEMENT: I have nothing to add.

DR. KROLL: Okay. Thank you. Let's go to question 5.

DR. PEACOCK: Question 5: Should the potential for bias by race, age, sex, hair color or other individual differences in the incorporation or retention of drug in the hair be evaluated? If yes, what additional studies should be requested?

DR. KROLL: Let's start with Dr. Kurt. Then we'll move counterclockwise.

DR. KURT: I think that it should to avoid discrimination problems under the Americans with Disabilities Act and other factors in the federal legislation. And I think that a point could be made in the hair testing that has been presented in the larger-n groups that there was no division by sex. As we know in the male population, most of us don't do anything to lighten our hair except when it gets gray. Women tend to lighten their hair, which, in general, I think probably removes some of their melanin, so that population might be somewhat skewed if included

in the population as a whole. So, I think further studies need to be done in this regard.

DR. KROLL: I tend to agree with Dr. Kurt. I don't think they have to be tremendously thorough studies, but there are a lot of women who dye their hair or change their hair color or do other things to it.

And as with respect to hair color, maybe do enough studies or put together the studies in such a way so that things related to the amount of melanin that's in the hair since that seems to be the main culprit. But even though I think that you probably have some evidence that the melanin's removed, but to make certain that that's very clearly stated what's going on and how that works.

DR. MANNO: I agree with Dr. Kroll. Nothing else to say.

DR. LEWIS: Sherwood Lewis. I have nothing to add.

DR. CLEMENT: Steve Clement. I think some of these should be done but possibly as post-marketing. From looking at it as best I can it looks

like, if anything, any of these variables would, if anything, decrease the sensitivity of the assay, so the bias would be against picking it up instead of for picking it up.

So, from that standpoint, if you still get a positive test, the person took heroin, period. There's no questions about it. It's just a matter of whether it picked me up or it picked up someone else. But if it is positive, I didn't see anything in the materials presented that showed that there would be a bias on causing a false positive, which is the biggest concern I had.

DR. HENDERSON: I think there's no question that studies need to be done to assess the influence of any of these demographic factors. And my concern is that it would discriminate against populations where perhaps the test was more sensitive; that is, that it's not that they didn't take it, it's just that their friends who did take it may be at an advantage of being able to treat their hair, wash their hair, do things, because their level was lower than when they started than other populations. And,

so I think there's no question it has to be studied.

I agree with Dr. Clement, it certainly could be post-marketing, perhaps, but definitely that data needs to be gathered.

To Mr. Reynolds' suggestion a couple of questions ago, there are populations that could easily be accessed to collect populations to look at these issues.

DR. ROSENBLOOM: I have nothing to add.

DR. LASKY: Fred Lasky. I agree that these are important studies that have sociological impact. I believe that the sponsor has shown, at least with reasonable assurance, that this is not a major issue, but I don't think that the specific questions which are important here have been addressed to the specifics. I would think that these studies would be done because of liability issues, and that would probably be the primary incentive. But I think it would be an important thing to do post-market.

MR. REYNOLDS: I pretty much agree with what everyone else has said, that the dyeing and treating and things of this nature seem to, if

anything, decrease the sensitivity, and you're not going to get false positives as a result. The demographic data should be collected. Once again, it can be collected post-market. This can be done fairly simply, and I don't think it would be too burdensome for the manufacturer to do that.

DR. EVERETT: James Everett. Certainly these items are necessary to be done, if for nothing other than to help prevent fraud and abuse. This is a test that stands at high potential for fraud and abuse as well as general accusations about who's used a drug, who hasn't used a drug.

Without doing these tests you will not know who the test is not suited for. If the test is suitable for young kids, the only way you're going to know is you have to check. If it's suitable or not suitable for elderly people because their chemistry changes quite a bit, and if you don't do the test, then you won't know. And these are just the fundamentals of all tests that should be done.

DR. WILKINS: Diana Wilkins again. I agree with the comments of Dr. Everett just a moment

ago. I think that the studies do need to be done. And the thing that I'm focusing in on, I think, is the individual differences in retention of drug in hair. And I think -- because I'm thinking of this as a potential application in a clinical setting.

The average hair growth rate, at least of what I've seen reported in the literature, is a huge range. And we've talked about earlier with the problems of using a mean data, a mean data point or a mean value. That can be problematic at times. I've seen anywhere in the literature from 0.6 to 1.3 centimeters per month. I don't know which number is valid, to tell you the truth, because it's from a wide range of studies. So, hair growth rate is important.

So, my question then is, well, if I'm going to rely on this to determine whether someone has stopped using heroin in a clinic or something like that, when am I going to be able to determine this? I would think hair growth rate would be somewhat important in that issue. When will a formally positive user become negative? Or if I keep testing them for six months, are they going to be positive for

six months whether they continue to use or not? I can't answer that question. I'm not saying that this test isn't sensitive enough to do that, but I don't know that I have the data to convince me that we can answer that type of question.

DR. KROLL: Okay. Let's go to question 6.

DR. PEACOCK: Question 6: Is the information provided by the sponsor adequate to address the issue of retention of drug in the hair from environmental exposure? If not, what additional information should be requested?

DR. KROLL: Let's start with Dr. Manno and move clockwise.

DR. MANNO: Barbara Manno. May I ask the sponsor a question --

DR. KROLL: Sure.

DR. MANNO: -- before I answer this? In your procedure, in processing the hair prior to the -- during the wash process, who determines or what determines what you're calling the short process and the long process? That wasn't exactly clear to me.

MR. IRVING: Right now, our standard

process is for all the samples to go through the entire wash procedure. We don't do a retest of the sample. We do an initial screening test. We do the extensive wash, digest our sample, do a confirmation, and apply the wash kinetics. And that's across the board for all our samples right now.

DR. MANNO: Then why do you have -- well, never mind.

MR. IRVING: Part of the reason that's in there is because some of the initial studies had some of that data in there also.

DR. MANNO: Oh, okay. But you are proposing it with that long process.

MR. IRVING: We're proposing that the single immunoassay followed by the extensive wash and the confirmation.

DR. MANNO: Okay, thank you.

DR. KROLL: Can you just give us your name, so we can --

MR. IRVING: Oh, John Irving, I'm sorry.

DR. MANNO: Barbara Manno again. I think that I'm satisfied with that wash procedure that

they've presented.

DR. KROLL: Martin Kroll. I'm basically satisfied. I would like to see when they do the analysis, the short analysis, against what they consider typical drug users, it would be nice to manipulate the data and show it against somebody who's right near the cutoff and what the effect is. I mean, again, when you're working with real problems, it's not the typical user. Where you get in trouble is somebody who's right close to a cutoff or whatever, and that presents issues and problems.

DR. KURT: Tom Kurt. I agree with both Dr. Manno and Dr. Kroll, and yes.

DR. WILKINS: Dr. Wilkins. I'm going to say in general yes with one exception. The only thing, and I'm not necessarily -- I'm just saying this as a possibility to be considered -- is that the effectiveness of the wash procedure and retention of drug in hair, the data looks very good what presented for -- the data that was in the submission looked very convincing.

But from my perspective is that most users

or heroin users it was soaked drug, and most heroin users are not soaking their hair in heroin solutions. And that's always been brought up as a limitation in the past for doing these type of studies is that that's not a really good -- it's not a realistic model for assessing environmental exposure.

Having said that, I think, if anything, it probably sort of pushes it to the one extreme where you would probably, if anything, be getting a lot of drug in there and challenging your system. But in reality and practice, I think people are being exposed to smoke and exposed to powder on hair, and I think that's a very different -- I think it's a different route or a different means of environmental contamination that the wash procedure would need to be addressed.

So, while the data that is submitted here using the soaked procedure does suggest to me that the washing procedure is quite effective, it would have been significantly enhanced in my mind and very convincing had there also been some data with hair that had been exposed to smoke or perhaps powder or

what have you. That would have really clinched it for me.

DR. EVERETT: James Everett. I particularly like the washing data, and that's kind of rare. But in reality, it does demonstrate that you can remove a consistent amount of drug from the hair before the actual specific test is performed at the end. And I think, again, it's very difficult to go through all of the possible environmental exposures that a person's hair could go through, particularly one who's using heroin. So, I'm satisfied with the data that they've already presented.

MR. REYNOLDS: Stan Reynolds. In addition to the experimental soaking, they also had the group of police officer, undercover police officers, who did have exposure to the environment in the testing that they did on them.

DR. WILKINS: That was a different drug. Wasn't that cocaine? That was a different drug. That's why -- I think that last study that the presenter showed this morning --

MR. THISTLE: Yes, Bill Thistle. That

study with the undercover narcotics officers was with cocaine, because that, in the literature, has always been the drug of issue. There really has been no literature expressing the fact that heroin is floating around or that people are soaking their heads in heroin. We did those as extreme contamination scenarios.

The real contamination scenario that has been brought has been brought with regards to cocaine, and that's why -- in fact, the articles that you've gotten about removal external contamination, both from the FDA and from Psychemedics, deal primarily with cocaine. The exception is the study that we did specifically for this assay where we soaked the hair and where we did the sweat contamination experiment.

DR. KROLL: Let's move on. Anymore comments?

MR. REYNOLDS: But just to finish up that point, in my limited experience in this area, if you're talking about environmental exposure, people who tend to spend a lot of time in shooting galleries, generally are not there as observers. So, I think

exterior contamination of hair is really not going to be a major issue.

DR. LASKY: Fred Lasky. I thought the data, as presented, were convincing, but there were a couple of things that I think are worth looking at with the data that's probably in the submission. And that is we saw the washing steps, and it was based on average data, based on my understanding of what I saw.

And I was intrigued by this extrapolation technique, which I thought was also very convincing. But the question that I would have is whether or not that extraction technique -- sorry, extrapolation technique compensates for the wash-to-wash variability that might be seen from sample to sample. I think the data probably contained in the submission.

And my suggestion would be that if it doesn't, that perhaps they extend the extrapolation technique out a little bit further if that is how to deal with that problem. But based on what I saw and the way it was presented, I thought the data were convincing.

DR. ROSENBLOOM: I agree.

DR. HENDERSON: I'd also agree.

DR. CLEMENT: I think the study was adequate. We hear all kinds of stories of people saying they use something they're caught with for various reasons. I remember in Newsweek, they said after the Olympics in Australia, the coaches found, what, 20 vials of growth hormone and they asked him what he was doing with it, and he said he uses it for his bald spot on his head, and he rubs it in his hair. So, I guess you never can be completely immune from what people will creatively come up with. So, I think it was a good study, and it proved a point, and there's no other further studies that need to be done.

DR. KROLL: Dr. Lewis.

DR. LEWIS: I'm sorry. I have nothing to add.

DR. KROLL: Okay. Let's go to question 7.

DR. PEACOCK: Question 7: Has the sponsor adequately demonstrated the effect of various washing or hair treatment procedures on the internally incorporated or bound drug? If not, what additional studies should be requested?

DR. KROLL: Okay, I'd like to start with Dr. Henderson, and then we'll go counterclockwise.

DR. HENDERSON: I was very impressed with the washing. And as a clinician, I think that I would be hard pressed to argue that there's an environmental risk to claiming someone's positive.

DR. ROSENBLOOM: Yes, I think that's probably true. There may be hair treatment modalities of which we are unaware, and I would expect some post-marketing further studies on whether one might be able to get a wash-out from very badly damaged hair. But I wonder if that kind of thing couldn't even be done in the laboratory without having to do it from a person's head.

DR. LASKY: Fred Lasky. I agree with Dr. Rosenbloom's comment that if this does become an issue, and I'm not convinced it will, but if it does, it could be easily handled in a post-market situation.

MR. REYNOLDS: Stan Reynolds. I have nothing further to add.

DR. EVERETT: James Everett. I agree. That's probably one of the better parts of the entire

study, I thought.

DR. WILKINS: I agree.

DR. KURT: Tom Kurt. I agree, in general. I would like to point out an issue that this is a kind of an ongoing process that makes this washing technique unique. The RIA technique is not necessarily unique, because it's been used in the drug testing industry, the laboratory testing industry for decades at this point. So, that's not the unique part of this process that's being reviewed.

I would like to point out as a footnote one of my concerns that I didn't mention this morning is the sodium azide reagent, which is 20 percent sodium azide, which is metabolized as cyanide in the body. It's quite a dangerous substance, and I've seen it used in our institution once by a pharmacologists on the faculty for suicide. And familiar with reports of it in the literature. It cannot be treated with a cyanide antidote kit, so it's a very dangerous substance and should be appropriately labeled.

DR. KROLL: Martin Kroll. I have no other additional comments.

DR. MANNO: Barbara Manno. I have no additional comments, but I have an additional question. I just happened to notice, as I was looking at the presentation of the wash on the -- it was question 6 in your presentation. I was looking at the numbers for your deriving the 28.4 milligrams. It's page -- I can't make out which page it is. It looks like page 11. As you've derived this final answer of 28.4 nanograms per ten milligrams of hair, I noticed that the test reports out on ten milligrams of hair, but you're weighing in eight. Do you do a massaging of the data there?

DR. CAIRNS: No. Again --

DR. KROLL: Please identify yourself.

DR. CAIRNS: Dr. Cairns again. The original screen is eight milligrams. Then if it is screened positive, it would move forward for washing and then digesting and confirmation. We do that on a weight basis.

DR. MANNO: So, how do you report it then?

DR. CAIRNS: Per ten milligrams.

DR. MANNO: But you started with eight

milligrams of hair in the analysis.

DR. CAIRNS: No. The first screen is eight. That's gone.

DR. MANNO: Okay.

DR. CAIRNS: Then we go back to the envelope and weight out a new amount, and then it's prorated per weight.

DR. MANNO: Gotcha. Thank you. That wasn't clear to me. Thank you.

DR. KROLL: Any comments? Dr. Lewis?

DR. LEWIS: Yes, to answer the question, I think that there has been an adequate demonstration of the effect of the washings.

DR. CLEMENT: I agree.

DR. KROLL: Okay, good.

Now, let me ask the FDA, do they think that we've commented sufficiently on these questions?

DR. GUTMAN: Yes.

DR. KROLL: Okay. Good.

DR. CAIRNS: Mr. Chairman, may I have your indulgence just for one moment?

DR. KROLL: Well, right before that, I

just want to ask if anybody else in the panel had any other short comments they wanted to make, and then we'll let you speak.

DR. WILKINS: Comments or questions?

DR. KROLL: Comments or questions but please keep them brief.

DR. WILKINS: A short one?

DR. KROLL: Yes.

DR. WILKINS: Just another clarification, just so I understand. On the wash procedure, I'm just a little confused. Again, this is all for me determining a positive or a negative and how that's occurring. Is the results of the final wash buffer subtracted from the quantitative mass spec result to determine a value that is then compared to your cutoff? And if so, is the wash analyzed by the semi-quantitative RIA or by the MS? I'm just not clear on it, and it doesn't really matter. I just wanted to make sure I understood.

MR. IRVING: When we do -- this is John Irving again -- when we do the wash, we do it by radioimmunoassay; however, we do a full curve on that

wash, and we do multiply that final value times five, subtracted from the digest, and compare it against the cutoff.

DR. KROLL: Okay. Any other additional comments?

You wanted to make a few additional statements?

DR. CAIRNS: It's very short.

DR. KROLL: At three o'clock, we do need to do the open public forum

DR. CAIRNS: It's Dr. Cairns again. For the record, I just feel it necessary to address a few points made during the discussion of the panel.

First of all, as regards additional information, such as regarding bias, et cetera, that's holding hair to a different standard than urine has been held traditionally.

And as regards to the demographics, I was sorry you had left the room when we addressed the issue, but it is in the attachment 21, 22, 23, as regards the individual studies A through E. There is demographic information contained in there.

And as regards the clinical standards for exclusion/inclusion, I repeat that Psychemedics just did not use that two parameter. We also used the fact that there was a negative urine and a negative hair test in some of those inclusion/exclusion criteria. So, we went beyond the standard as presented in the questions. Thank you.

DR. KROLL: All right. Thank you, everybody, very much.

We need to do the open public hearing at three o'clock, and now it's about five minutes to three. I suggest we forego the break and do the open public hearing now.

Okay, so we're going to hear from Rosemary Mumm.

MR. MUMM: Yes, thank you for inviting me and letting myself be invited.

I'm presenting the practioners' point of view for hair testing, and we've had some experience, obviously, with heroin. I'd like to also, in general, though, address my comments to technology.

I see there's a note here that if we have

any financial obligations or indebtedness to Psychemedics that they need to be stated. We do not. As the DA's office, we in fact have a high accounts payable with them, and we feel it's well worth it.

I'm the Director of the Diversionary Programs, and I have been for eight years with the New Orleans District Attorney's Office. The Diversion Program is an alternative to prosecution program for new offenders. These are both juvenile and adult folks who've been arrested on both narcotics and non-narcotics charges. They're all non-violent offenders.

I've been using hair testing for eight years to monitor the people in our program to determine whether they need to be in a counseling track for substance abuse or a counseling track for some other mental health or clinical issue.

We assess them, if they are in a drug-free track, to become -- in a drug counseling track, to become drug-free. That is our intent and our motive. I'm not trying to find reasons to put people in prison. I'm trying to find reasons to assist them to deal with their drug problem so that they don't repeat

their criminal offenses. Now, we are very effective, by the way, in reducing criminal recidivism.

Our population -- I know that's been a big issue today -- ranges from the ages of 12 to 66. We are primarily an African-American city by about 65 percent, and the population in our program reflects that demographics data for the city. Primarily two-thirds of the people are male, and complimentary, a third are female.

My background has been 20 years in the field of substance abuse treatment. In the last ten years, that has been the context of criminal justice. Someone asked what the BCSAC is behind my name, and that's Louisiana credential, a Board-Certified Substance Abuse Counselor.

In addition to the Diversionary Program role that I have, I've been assisting with my boss, Harry Connick, the District Attorney, in helping to implement high school drug testing programs, and I'll talk a little bit about that.

We began our program eight years ago through funding from the Department of Justice,

specifically to look at hair testing to monitor offenders in a supervisory program. Was it effective? Did it work? How did we feel about it? We've used Psychemedics technology during that whole time.

I believe that the program is so -- the technology, hair testing, is so vital in our success that should I go to another program and continue in substance abuse treatment, I cannot imagine myself doing treatment anymore without hair testing. For us, a piece of hard evidence or as hard of evidence as one can get in an imperfect world about whether someone is using drugs or not.

We also used urinalysis. We want the benefits of both technologies -- the longer-term window of detection as well as determining whether someone has recently used drugs. We use hair testing when someone is first assessed when they get into our program to determine, as I said before, what kind of counseling track they go into.

We have a lot of people who are arrested on non-narcotics charges who deny drug use. And perhaps about half of those, when we administer a hair

test, come back with a positive result. Now, had we not done that and only used urine, I would predict that that would be much lower, because we have scheduled appointments with people. They know when they're coming in, and they would know then that if they were to be drug tested that many of those could refrain from use for a day or two.

Again, we also use the hair testing to monitor their three to 15 months in our program. It allows us to decrease the number of urine tests that we do and thus the cost of urine testing. We really are monitoring whether someone is remaining drug-free as a part of their treatment program. We would have to be urine testing maybe three times a week, which would get enormously expensive for us.

With the kind of 24-hour tape recording that the hair offers for us, we can reduce that frequency and still periodically do a hair test to see if they're remaining drug-free. But I wouldn't abandon urine testing. It's really important to know whether someone has used today or yesterday or some recent -- had some recent use.

In addition, we like the advantages of the collectionees. Certainly, my staff dislike collecting urine samples. They don't mind doing hair sample collections. We like the retest capabilities when a result is challenged. And again for other reasons, observing urine collections, the frequency of being able to do a hair test rather than the high volume manual labor-wise of doing random urines is greatly beneficial to our program.

We have a very high level of confidence in its detection abilities. Our staff rates heroin detection in hair as excellent, in light of the self-report of the person being tested, their arrest history, and their urinalysis results. Fortunately, in our 12 to 16 age population, which is our juvenile program, we have had no self-reported heroine users nor any positive hair tests, nor positive urine tests, I might add. In my experience, though, beginning with some of our arrestees at age 17, we've seen some very, very serious heroin users who apparently just hadn't been arrested before their 17th birthday.

For us, and this is not related to heroin

use as this hearing has directed, but the recent addition of MDMA in the panel has been very welcome because of the expensive urine testing for MDMA, which we would not be able to afford otherwise. And in New Orleans there's been quite a number of young people who have either died or have had medical emergencies, severe medical emergencies for which we now feel we have a tool to assist with that intervention.

As far as the high school drug testing goes in New Orleans, there are now ten schools in New Orleans that have adopted drug testing programs using hair. A number of other principals, because of the success of these schools, have stepped forward and are looking for money so that they can adopt similar programs.

The principals have said, those who've used hair testing in their schools, that they've seen disciplinary and behavioral problems drop. The school milieu has changed, the student attitudes have changed, and they feel that this has been a real positive addition to what's happening in the schools.

Last week, one of the principals who's

been doing testing for over three years now, reported that they had tried urine testing. They knew they had a big drug problem in their school -- I don't think she'd mind if I mentioned the school, called De La Salle High School, known in the community as De La Drug High School prior to beginning hair testing -- and found that urine testing was not effective in turning their school around with their drug use problems.

They gave a 90-day warning to their students and the parents. This is a private school, so they had the constitutional right to test all their students. The first year they had a 3.4 percent positive rate. The second year went to 2.1. And year three was less than one percent. I think their population is about 850 students.

They feel it has a very strong deterrent effect in not only discouraging kids from using drugs but also in identifying those few kids who did have a positive detection to get them into counseling and treatment.

All these high school programs are

intended as student assistant programs and not punitive programs.

And last week, finally, my boss and I testified before the -- well, spoke before the mayor's Subcommittee on Violence in the Schools. We had a shooting, like many other high schools in the country. As a result of that, this Subcommittee was formed. And the Subcommittee agreed that it would propose to the mayor and city council to seek advocacy from the top administration to look to the public schools to adopt more testing in the programs and endorsing hair testing as the method.

All I can say in summary is that as a clinician and someone whose motivation is to get people into the proper services to turn their lives around, I can't say enough about hair testing. It's not a perfect technology. Certainly, we've had people who have challenged the results in our program, people who care not to admit that they're using but when confronted with results 90 percent of the time or higher admit to doing that.

We have power over the situation, unlike

a pregnant mother who would want to come forward with acknowledgement of drug use as a step and where the DA's office -- these are people who are not motivated to reveal their drug use, knowing full well that if they did it may jeopardize their court case and potentially land them in jail.

That's all I have.

DR. KROLL: All right. Thank you.

All right. What did you want to do now? Do you think it's pertinent, Dr. Gutman, to ask her questions from the panel?

DR. GUTMAN: Certainly. There's no reason you couldn't.

DR. KROLL: Okay.

DR. LEWIS: Sherwood Lewis. I had one quick question for you. And I'd like to know what the rationale and the ramifications for doing drug testing in those individuals who are arrested or apprehended for non-drug related offenses?

MR. MUMM: Well, it's my belief that if someone is arrested on a theft charge, for example, there may in fact be an underlying substance abuse

disorder. We know that people who are needing money for drugs resort to thefts and other criminal activities to get money for their drugs.

We want to screen -- when we put someone in an appropriate counseling program, the priority is first to get them drug-free if they are abusing drugs. Then if there are other family issues, mental health issues, that can be worked in accordance with the drug treatment program. But unless we serve to help that person get off of drugs, I personally would expect that that criminal activity would continue.

DR. LEWIS: I guess my question goes to the point of whether an individual voluntarily subjects himself or herself to that --

MR. MUMM: Yes, it's a voluntary program, yes.

DR. LEWIS: -- testing, even though they've been arrested for something not connected with the crime.

MR. MUMM: Right.

DR. LEWIS: So, the volunteer to --

MR. MUMM: Yes.

DR. LEWIS: -- do this.

MR. MUMM: Yes, they can enter the program or they can go to court and face the charges there. So, it has some coercive elements to it.

DR. LEWIS: They enter the program, but they enter the program subsequent to their having been tested positive.

MR. MUMM: No, they enter the program whether they're using drugs or not, if they choose to, do so. Once they sign in and we take a hair test, then that determines what type of program we would ask them to participate in.

DR. LEWIS: So, they sign on to the program, then you folks do the testing.

MR. MUMM: Right, and we tell them, though, when they sign in they know that they will be hair tested.

DR. LEWIS: Thank you.

DR. KURT: Could I ask a quick question? Is there a consent form that they sign when they give the specimen or is it an order from the court that they give a specimen?

MR. MUMM: No, it's a consent form. There's no court order involved.

DR. KROLL: All right. Does anybody else from the public wish to speak? Okay.

Dr. Gutman, do you have any questions or concerns or any comments you want to make?

DR. GUTMAN: No, I don't.

DR. KROLL: All right. I was talking to our executive secretary, and she said, well, I could summarize what our comments were. I think it's rather difficult to summarize them, because for many of the questions I think you heard divergent opinions. And some of them you heard a lot of agreement. But I'd certainly open it up to the panel if anybody wants to make a closing comment or something else pertinent to the questions that they have to ask.

DR. HENDERSON: I think in summary we all are excited about the technology and would certainly urge that it be marketed soon, although we do have reservations and perhaps many of those, if not all of those, could be addressed in post-market study.

DR. KURT: As a medical review officer,

I'm certainly looking forward to hair testing that can be performed under direct observation rather than having urine testing performed, for it's so easy to cheat. However, I think that the problematic areas that we pointed out today should be remedied, and some of it can be done on a post-marketing basis.

DR. KROLL: Anybody else have any other comments?

MS. CALVIN: I just wanted to make some closing remarks. Thank you, Psychemedics, FDA staff, and the panel, of course, for all of your recommendations. And the next tentative meeting for the Clinical Chemistry and Clinical Toxicology -- how could I forget Toxicology -- Devices Panel will January 17, 2001.

DR. KROLL: I'd like to also thank the members of the panel, the FDA staff, both from Psychemedics and other people who have made comments for today.

Did you want to make any closing comments, Dr. Gutman?

DR. GUTMAN: No. I'll add my thanks to

yours.

DR. KROLL: Okay. So, we now can adjourn the meeting.

(Whereupon, the FDA Meeting was concluded at 3:18 p.m.)

CERTIFICATE

This is to certify that the foregoing transcript in the matter of: MEETING

Before: CLINICAL CHEMISTRY AND CLINICAL TOXICOLOGY DEVICES PANEL

Date: NOVEMBER 14, 2000

Place: GAITHERSBURG, MARYLAND

represents the full and complete proceedings of the aforementioned matter, as reported and reduced to typewriting.

Rebecca Davis